washed and then were embedded in cinnamic acid matrix as described above. The matrix eluted peptides were analyzed for mass spectrometry, as shown in **FIG. 4B**. The epitope containing tryptic peptide was identified using the pepident program from the EXPASY suite. For the control experiment HA-tagged transferrin receptor expressed in CHO cells was immuno-precipitated using anti-HA IgG coupled to sepharose beads. The purified protein was displaced from the beads using HA-peptide and then digested with immobilized TPCK-treated trypsin. The scFv epitope-containing peptide was purified using the H7 scFv and analyzed for mass as above and is shown in **FIG. 4C**. The transfected transferrin protein contain an HA epitope sequence on it's amino terminal (intracellular domain). This tag serves as a control for extracellular-specific labeling.

[0159] Trypsin digests of the purified transferrin receptor and of the cell surface proteins were labeled with the primary amine reactive dye NHS-CY-5 and dialyzed against PBS. The labeled peptides were then diluted to a concentration of 0.2 mg/ml in PBS with 10 mg/ml BSA and 0.05% Tween 20 and incubated on the surfaces of glass slides which had been derivatized with the scFv against the transferrin receptor (H7). Incubations were performed overnight in a humidified chamber at 4° C. Binding of CY-5 labeled peptide was determined using a fluorescence scanner. **FIG. 4D** shows the result of the experiment where the transferrin receptors are shown to bind to the H7 scFv of varying concentrations. Because the HA epitope was on an intracellular domain, the anti-HA IgG serves a negative control here.

[0160] (ii) Functionality Testing of scFv Coupled to Maleimide-Derivatized Glass Slides

[0161] Spots on a maleimide-derivatized slide surface were outlined with a hydrophobic pen to keep samples from spreading and 1.0 μg of scFv reduced as described in Example C (ii) was then allowed to couple to the glass surfaces for 12 hours at 4° C. in a humidity chamber. The thiolcontaining terminal cysteines readily attach to the maleimide groups, presumably by a thioether linkage. Monoclonal antibodies to cytochrome-c and Bcl-2, and scFv without terminal cysteines were treated with 2-iminothiolane.HCI (Traut's reagent) to introduce sulfhydryl residues at surface-exposed lysines. These antibodies were then reduced as described above and used as controls. After coupling, the spots were rinsed 3× with PBS containing 2% BSA, 0.05% Tween 20, and 1.0 mM β-mercaptoethanol for 15 minutes at 25° C. Cognate ligand or negative control were added to the appropriate spots at concentrations ranging from 10.0 pM to 0.01 pM in PBS containing 2%BSA, 0.05%, Tween-20 and allowed to incubate for 2 hours in a humidity chamber at 4° C.

[0162] In some cases, 40% glycerol is added to the spotting mixture to facilitate the microarraying of the scFv's, because the samples will not dry out even when spotted in submicroliter volumes. For scFv C6.5 and scFv F5, 40% glycerol had no adverse effect on the function of the scFv binding.

[0163] The cognate ligand for scFvC6.5 is the purified erbB-2 receptor. The recombinant ectodomain of erbB-2 was expresssed and purified from CHO cells using standard techniques. NHS-CY5 monofunctional dye (AMERSHAM) was used to label the protein at a final molar dye/protein ratio of 5.0. The labeling reaction was carried out in 0.1 M sodium carbonate buffer for 30 minutes at 25° C. and exchanged into PBS using a P10 spin column. Other proteins used as controls (Bcl-2, cytochrome-c, and BSA) were similarly labeled with CY5 as described. Labeled proteins were examined for immunogenicity by immuno-precipitation either with phage generated antibody or monoclonal antibodies and were then used as ligands to glass coupled scFv. The erbB-2 proteins were incubated in a range of 1 uM to 1 pM in PBS Tween 20 with 2% BSA for 2 hours at 25° C. in a humidity chamber. CY5 labeled erbB2 was used as a negative control.

[0164] After incubation, samples were washed 3×2 minutes with PBS, 0.05% Tween 20 and 1× with PBS. Samples were allowed to dry and then imaged on a molecular dynamics STORM using the excitation at 640 nm.

[0165] (iii) Small Molecules in Signal Transduction

[0166] Recombinant fusion proteins from the Bcl-2 family of apoptosis regulating proteins were prepared by standard methods and printed on either BSA-NHS glass slides or an aldehyde derivatised glass slide. Proteins were printed at concentrations ranging from 200 to 20 micrograms per milliliter in a buffer containing 40% glycerol. Printing was performed as described using the GMS 417 ring and pin printer. Plates were loaded with the capture protein samples; 96 well plates for printing with the GMS417 printer. Proteins were allowed to incubate on the reactive slides for 12 hours under slightly hydrated conditions at 4° C. After the binding reaction went to completion the slides were rinsed with PBS and variations of the cognate ligand labeled with fluorescent dyes. Detection was performed using the Arrayworx optical reader.

[0167] The printed proteins were GST fusions of Bcl-XL and BAX and a 6× histidine-tagged-Bcl-XL. Ligands for these proteins were the full length Bcl-XL protein and the BH3 containing peptide from the Bcl-2 family protein BAK. The peptides were labeled with Alexa 488 and the full length protein was labeled with CY5. The volume of liquid delivered from the GMS printer is 50-70 pL per stroke repeated 5 times. Protein delivered ranged from 350 pg to 350 fg of protein per spot. After printing, proteins were allowed to incubate for 12 hours at 4 degree in a humidity chamber. The slides were then washed with PBS and blocked with PBS with 10% BSA for 5 minutes. To determine the reactivity of the surfaces and the coupling efficiency of the proteins, the presence of the GST-fusion proteins were monitored using labeled anti-GST-tag antibody at 1 ng/ml.

[0168] Labeled protein ligands were incubated in a volume of 40 μl contained in an area of 1 cm^2 by a hydrophobic barrier.

[0169] The slides were then rinsed and read using the Arrayworx scanner. In addition, As shown in **FIG. 5**, which is a mass spectrometry profile, binding of a ligand by a Bax-GST protein is confirmed on the left, while non-binding by a GST protein is shown on the right.

[0170] **FIG. 6** confirms the ability of an unlabelled small molecule (a BH3 peptide here) to compete a labeled ligand (Bcl-XL here) off the capture molecule (Bax-GST fusion protein). As shown in the four mass spectrometry profiles, with an increasing amount of the BH3 peptide, lesser binding between labeled ligand and the capture protein was